

# PATENT COOPERATION TREATY

## PCT

### INTERNATIONAL PRELIMINARY REPORT ON PATENTABILITY (Chapter II of the Patent Cooperation Treaty)

REC'D 14 MAR 2005

PATENTABILITY PCT

(PCT Article 36 and Rule 70)

Applicant's or agent's file reference 4-33172A	<b>FOR FURTHER ACTION</b>	
See Form PCT/PEA/416		
International application No. PCT/EP2004/003980	International filing date (day/month/year) 15.04.2004	Priority date (day/month/year) 16.04.2003
International Patent Classification (IPC) or national classification and IPC C07D207/16, A61K31/401, A61P3/10		
Applicant NOVARTIS AG		

1. This report is the international preliminary examination report, established by this International Preliminary Examining Authority under Article 35 and transmitted to the applicant according to Article 36.
2. This REPORT consists of a total of 4 sheets, including this cover sheet.
3. This report is also accompanied by ANNEXES, comprising:
  - a.  (*sent to the applicant and to the International Bureau*) a total of sheets, as follows:
    - sheets of the description, claims and/or drawings which have been amended and are the basis of this report and/or sheets containing rectifications authorized by this Authority (see Rule 70.16 and Section 607 of the Administrative Instructions).
    - sheets which supersede earlier sheets, but which this Authority considers contain an amendment that goes beyond the disclosure in the international application as filed, as indicated in item 4 of Box No. I and the Supplemental Box.
  - b.  (*sent to the International Bureau only*) a total of (indicate type and number of electronic carrier(s)), containing a sequence listing and/or tables related thereto, in computer readable form only, as indicated in the Supplemental Box Relating to Sequence Listing (see Section 802 of the Administrative Instructions).
4. This report contains indications relating to the following items:
  - Box No. I Basis of the opinion
  - Box No. II Priority
  - Box No. III Non-establishment of opinion with regard to novelty, inventive step and industrial applicability
  - Box No. IV Lack of unity of invention
  - Box No. V Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement
  - Box No. VI Certain documents cited
  - Box No. VII Certain defects in the international application
  - Box No. VIII Certain observations on the international application

Date of submission of the demand 27.10.2004	Date of completion of this report 11.03.2005
Name and mailing address of the International preliminary examining authority:   European Patent Office D-80298 Munich Tel. +49 89 2399 - 0 Tx: 523656 epmu d Fax: +49 89 2399 - 4465	Authorized Officer  Menegaki, F Telephone No. +49 89 2399-8277



# INTERNATIONAL PRELIMINARY REPORT ON PATENTABILITY

International application No.  
PCT/EP2004/003980

## Box No. I Basis of the report

1. With regard to the **language**, this report is based on the international application in the language in which it was filed, unless otherwise indicated under this item.
  - This report is based on translations from the original language into the following language, which is the language of a translation furnished for the purposes of:
    - international search (under Rules 12.3 and 23.1(b))
    - publication of the international application (under Rule 12.4)
    - international preliminary examination (under Rules 55.2 and/or 55.3)
2. With regard to the **elements\*** of the international application, this report is based on (*replacement sheets which have been furnished to the receiving Office in response to an invitation under Article 14 are referred to in this report as "originally filed" and are not annexed to this report*):

### Description, Pages

1-11 as originally filed

### Claims, Numbers

1-14 as originally filed

- a sequence listing and/or any related table(s) - see Supplemental Box Relating to Sequence Listing

3.  The amendments have resulted in the cancellation of:
  - the description, pages
  - the claims, Nos.
  - the drawings, sheets/figs
  - the sequence listing (*specify*):
  - any table(s) related to sequence listing (*specify*):
4.  This report has been established as if (some of) the amendments annexed to this report and listed below had not been made, since they have been considered to go beyond the disclosure as filed, as indicated in the Supplemental Box (Rule 70.2(c)).
  - the description, pages
  - the claims, Nos.
  - the drawings, sheets/figs
  - the sequence listing (*specify*):
  - any table(s) related to sequence listing (*specify*):

\* If item 4 applies, some or all of these sheets may be marked "superseded."

**INTERNATIONAL PRELIMINARY REPORT  
ON PATENTABILITY**

International application No.  
PCT/EP2004/003980

**Box No. V Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement**

**1. Statement**

Novelty (N)	Yes:	Claims	1-14
	No:	Claims	
Inventive step (IS)	Yes:	Claims	
	No:	Claims	1-14
Industrial applicability (IA)	Yes:	Claims	1-14
	No:	Claims	

**2. Citations and explanations (Rule 70.7):**

**see separate sheet**

**INTERNATIONAL PRELIMINARY  
REPORT ON PATENTABILITY  
(SEPARATE SHEET)**

International application No.  
**PCT/EP2004/003980**

(V)

Having regard to the International Search Report the claimed process involving DMF and avoiding the isolation of 1-chloroacetyl-2-cyanopyrrolidine in reaction step (b)/(c) differs from documents

- (D1) WO 98/19998, in particular steps 1,2 on p.8 and the examples;
- (D2) WO 00/34241, Ex.1B therein;
- (D3) WO 01/96295, in particular reaction scheme on p. 11 and Ex.1A therein;
- (D4) US-A-6380398, in particular col.13, l.24-30 therein;
- (D5) Tetrahedron, vol.58, 2002, p.5741-5746, in particular p.5741 therein due to the THF and TFAA involved in said prior art processes.

The requirements of Art.33(2) PCT appear therefore to be fulfilled.

The problem to be solved is considered to be the provision of a novel preparation process for compounds of formula (I) allowing to recycle all solvents and suitable for industrial production.

The present solvent and dehydrating agent DMF was not disclosed in the prior art (D1) to (D3), wherein TFAA was involved in the preparation examples. Nevertheless, the role of DMF in this respect is generally known to the skilled man, as mentioned in (D4), col.13, l.24-30 therein, and the skilled man seeking to avoid removal of TFAA and isolation of intermediate 1-chloroacetyl-2-cyanopyrrolidine would have introduced an alternative agent such as DMF. Therefore, Claims 1-7 lack inventive step. Moreover, even if the Applicant could show the involvement of inventive step for Claims 1-7, the compositions according to Claims 8-14 could not be regarded as inventive since they do not belong to the same inventive concept with the claimed process and they are not inventive over the prior art. The requirements of Art.33(3) PCT do not appear to be fulfilled.

The substituents R'/R" in formula (IB) on p.7 appear to correspond to R'''/R'''".